REMARKS

Claims 78-99 are pending in the application. Claims 98 and 99 have been amended by rewriting them in independent form. The amended claims are completely supported by the application as filed and do not raise any issue of new matter. Claims 78-97 are canceled without disclaimer or prejudice to Applicants' right to pursue the subject matter of one or more such claims in a continuing or divisional application. New claims 100-116 are added. Support for these claims may be found, inter alia, in the specification as follows: claim 100: page 22, lines 5-11; claim 101: page 17, lines 20-24, page 15, lines 5-6, page 22, lines 16-24, page 23, lines 15-17 and 22-25; claim 102: page 22, lines 13-14; claim 103: page 23, lines 6-17; claim 104: page 22, lines 28-30; claim 105: page 15, lines 9-13; page 17, lines 20-35; page 18, lines 23-24; page 33, lines 25-37; page 37, lines 21-22; Figures 3, 4, 5B, 6A and 6B; claim 106: page 15, lines 9-13; page 17, lines 20-35; page 18, lines 23-24; page 33, lines 25-37; page 37, lines 21-22; Figures 3, 4, 5B, 6A and 6B; claim 107: page 14, lines 30-31; claim 108: page 14, lines 32-33; claim 109: page 12, lines 21-23, page 33, lines 26-27; claim 110: page 22, lines 5-11; claim 111: page 22, lines 13-14; claim 112: page 23, lines 6-17: claim 113: page 22, lines 28-30; claim 114: page 14, lines 30-31; claim 115: page 14, lines 32-33 and claim 116: page 15, lines 8-12, page 17, line 20 through page 18, line 2 and page 19, lines 10-13. Furthermore, support for the recitation of "fragments" of the subject antibodies throughout the claims is present at page 14, lines 26-30 and page 19, lines 18 and 23. Thus, there is no question of new matter with regard to claims 100-116. Entry of this Amendment is therefore respectfully requested such that claims 98-99, as amended, and new claims 100-116 will be pending.

Sequence Compliance

The Examiner stated that this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. §1.821(a)(1) and (a)(2). The Examiner also stated, however, that this application fails to comply with the requirements of 37 C.F.R.§§1.821-1.825 for the reasons set forth on the Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures ("Notice to Comply") provided as an Attachment to the Office Action.

In response to the Examiner's objections Applicants submit that, pursuant to the regulations of the Office, they are filing on of even date herewith a separate response to the Notice to Comply addressed to: Assistant Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 2327, Arlington, VA 22202, Attn: Box Sequence. This Response addresses all of the issues raised in the Notice to Comply and thus the Examiner is respectfully requested to reconsider and withdraw her objections under 37 C.F.R. §§1.821-1.825.

Election/Restrictions

The Examiner stated that Applicants' election of Group V and species PA 14 with traverse is acknowledged. The Examiner stated that restriction between the humanized and non-humanized monoclonal antibody forms is withdrawn, and therefore, all pending claims 78-99 are under consideration. The Examiner stated further that should the elected species PA14 be free of prior art, a subsequent search for the other species will ensue.

In response, Applicants submit that pending claims 78-97 are canceled without disclaimer or prejudice. Claims 98-99 have been rewritten in independent form and, as amended, are believed to be in condition for allowance for the reasons set forth on p. 10 of the Office Action, as discussed further below. In addition, new claims 100-116 have been added. These new claims are directed to the same, i.e., Group V, invention, which claims more clearly recite the subject matter which Applicants wish to patent at this time. These new claims are believed to meet all of the requirements for patentability and thus to be in condition for allowance.

Objection to the Specification

The Examiner stated, on p.2 of the Office Action, that the Abstract of the Disclosure is objected to because it must be 150 words or less and that correction is therefore required. Citation is made to M.P.E.P. Section 602(i).

In response to this objection, the Examiner is respectfully requested to substitute the Abstract filed with the application with the Abstract of the Disclosure provided herewith as **Exhibit A.** The replacement Abstract substituted herewith is believed to overcome the grounds for objection and the Examiner is thus respectfully requested to reconsider and withdraw the objection to the abstract.

Objection to the Drawings

The Examiner stated, at pp.2-3 of the Office Action, that the drawing of Figure 4 is objected to because the numbers in the boxes are very hard to read. The Examiner stated that a proposed drawing correction or corrected drawings are required in reply

to the Office Action to avoid abandonment of the application. The Examiner stated that the objection to the drawing will not be held in abeyance.

In response to the objection to Figure 4, Applicants submit herewith as **Exhibit B** for the Examiner's approval a proposed replacement Figure. To avoid further difficulty in viewing the numbers in the respective boxes due to shading of the boxes, Applicants have replaced the shading with cross-hatching. Thus the information conveyed by the replacement Figure remains unchanged from the original; it is only the presentation of that information that has changed to render the subject Figure more easily readable.

The Examiner is therefore respectfully requested to approve the proposed replacement for Figure 4 to permit its entry into the file of this application.

Claim Objections

The Examiner stated on page 3 of the Office Action that claims 88, 89 and 98 are objected to because "P11" is presumably "PA11". The Examiner additionally stated that appropriate correction is required.

In response, Applicants note that the cancellation of claims 78-97 renders moot the objection to claims 88 and 89. Claim 98, as amended (i.e., rewritten in independent form), now recites "PA11" (emphasis supplied). This amendment is believed to overcome the objection to claim 98.

Allowable Subject Matter

The Examiner stated on page 10 of the Office Action that claims 98 and 99 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and upon satisfaction of all deposit and availability requirements under the Budapest Treaty. The Examiner further stated that claims 98 and 99 are drawn to allowable subject matter because the prior art does not teach or suggest the instant monoclonal antibodies or the hybridomas producing the antibodies. The Examiner stated that these claims (i.e., 98 and 99) would be allowable if claim 98 were drafted in independent form.

In response, Applicants submit that claims 98 and 99 have been amended such that they are now written in independent form. Moreover, as disclosed in the paragraph bridging pps. 13-14 of Applicants' specification, the hybridomas producing the monoclonal antibodies PA8, PA9, PA10, PA11, PA12 and PA14 have been deposited pursuant to and in satisfaction of, the requirements of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure with the American Type Culture Collection (ATCC) under following Accession Nos. ATCC Accession No. HB-12605 (PA8), ATCC Accession No. HB-12606 (PA9), ATCC Accession No. HB-12607 (PA10), ATCC Accession No. HB-12608 (PA11), ATCC Accession No. HB-12609 (PA12) and ATCC Accession No. HB-12610 (PA14). All restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent (37 C. F.R. § 1.808 (a) (2)). Therefore, claims 98 and 99, as amended, are believed to be in

condition for allowance.

Double Patenting Rejections

The Examiner stated that claims 78-88 and 90-98 are provisionally rejected under the judicially created doctrine of double patenting over claims 78, 79 and 80, respectively, of copending Application No. 09/464,9052 [sic 09/464,902]. The Examiner stated that this is a provisional double-patenting rejection since the conflicting claims have not yet been patented. The Examiner further stated that the subject matter claimed in the instant application is fully disclosed in the referenced co-pending application and would be covered by any patent granted on that copending application since the referenced co-pending application and the instant application are claiming common subject matter as follows: monoclonal antibody PA14 and any other antibody that bonds to the same epitope as PA14. The Examiner also stated that there is no apparent reason why Applicants would be prevented from presenting claims corresponding to those of the instant application in the copending application.

In response to the double patenting rejection, Applicants respectfully traverse the Examiner's statement that copending application Serial No. 09/464,902 and the instant application are claiming common subject matter. In response to a Restriction Requirement issued by the Office for application Serial No. 09/464,902 on September 25, 2001, Applicants filed an Amendment In Response to the subject Office Action on March 25, 2002 electing, with traverse, the claims of Group VI (nos. 87-88) drawn to nucleic acids encoding CDR regions of an anti-CCR5 monoclonal antibody. Furthermore, new claims 91-101 all directed to nucleic acids, were added to the copending application. Thus, the claims under consideration by the Examiner in application

Serial No. 09/464,902 are, as noted, directed to nucleic acids. In contrast, the claims of the present application are directed to monoclonal antibodies and not nucleic acids.

For the reasons above, therefore, the double-patenting rejection is believed to have been overcome and the Examiner is respectfully requested to reconsider and withdraw the subject rejection.

Claim Rejections Under 35 U.S.C.§112, Second Paragraph

The Examiner stated, on page 4 of the Office Action, that claims 93 and 95-97 are rejection under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Examiner further stated that claim 93 is vague and indefinite because the metes and bounds by what is intended or encompassed by "some, most or all of the amino acids" in lines 1-2 and 4-5 of the subject claims can not be determined. In response, Applicants submit that the cancellation of claim 93, without disclaimed or prejudice, renders this rejection moot. Further, none of the amended claims 98-99 or new claims 100-116 contain the language in question. Thus this ground for rejection is not relevant to any of the presently pending claims.

The Examiner also stated that claims 95 and 96 state that the donor immunoglobulin comprises "the CDR's" and asks "which CDRs" are being referred to? Applicants submit, however, that the cancellation of the subject claims, without disclaimer or prejudice, renders the rejection of claims 95 and 96 moot.

The Examiner additionally stated that claims 96 and 97 are confusing because claim 96 stated that the framework of a donor immunoglobulin is murine in claim 97. The Examiner thus inquired whether the framework of the antibody is derived from human, except for the murine amino acids immediately adjacent to the CDR's, or whether there can be two possible donors for each humanized antibody, i.e., one from human and another from murine? In response, Applicants submit that the cancellation of claims 96 and 97, without disclaimer or prejudice, from the application renders moot the rejection of those claims.

For the reasons discussed above, therefore, the Examiner is respectfully requested to reconsider and withdraw the rejections of Applicants' claims based upon 35 U.S.C.§112, ¶2.

Rejections Under 35 U.S.C. §112, First Paragraph

Claims 88, 89 and 98 are rejected under 35 U.S.C.§112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner stated that it is apparent that hybridomas to make monoclonal antibodies PA8-PA12 and PA14 are required to practice the claimed invention because they are necessary limitations for the success of the invention as stated in the claims. The Examiner stated that as a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. The Examiner stated that if it is not so obtainable or available, the enablement requirements of 35

U.S.C. §112, first paragraph, may be satisfied by a deposit of the hybridomas that make monoclonal antibodies PA8-PA12 and PA14, citing CFR 1.802.

The Examiner stated that the specification does not provide a repeatable method for obtaining the hybridomas that make monoclonal antibodies PA8-PA12 and PA14 and it is not apparent if it is readily [available] to the public. The Examiner stated that Applicant's deposit statement on specification pages 13-14 does not indicate the extent of public availability. The Examiner stated that if the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements, citing CFR 1.808.

In response to the above rejection under 35 U.S.C.§ 112, ¶1, Applicants note that claims 88 and 89 have been canceled from the application, without disclaimer or prejudice, thus rendering moot the rejection of those claims.

As to claim 98, the subject claim, as amended, is believed to overcome the rejection under §112, ¶1. That is, as noted above in the discussion headed, "Allowable Subject Matter", the Examiner stated on page 10 of the Office Action that claim[s] 98...[is] drawn to allowable subject matter because the prior art does not teach or suggest the instant monoclonal antibodies.... Following this statement the Examiner went on to state that,

"These claims would be allowable if claim 98 were drafted in independent form". Thus, the amendment of claim 98 to redraft the subject claim in independent form, taken together with the attorney of record's statement on page 11 above verifying that the hybridomas producing the antibodies were deposited as per the requirements of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent (37 C.F.R. § 1.808 (a) (2)), is believed to overcome the rejection of the subject claim under §112, which rejection should therefore be reconsidered and withdrawn.

Rejection Under 35 U.S.C.§102

Claims 78-88, 90, 91, 93, 94 and 97 are rejected under 35 U.S.C.§102(a) as being anticipated under Wu et al.(WO 98,18826) ("Wu et al. I").

The Examiner stated that the claims are drawn to a monoclonal antibody that binds to the N-terminus and/or one of three extracellular loops of CCR5 and is humanized by incorporation of a human immunoglobulin framework.

The Examiner stated that Wu et al. I teaches that monoclonal antibodies 5C7 and 3A9 are both specific for the N-terminus of the CCR5 receptor and monoclonal antibody 2D7, which was generated from murine IgG1, has epitope specificity for the second extracellular loop of CCR5 (see page 15, line 27 to page 6, line 5). The Examiner also stated that the subject reference further teaches humanized forms of the antibodies, where the framework and the consensus are derived from a human immunoglobulin or multiple immunoglobulin molecules, where the regions surrounding the CDR regions have been replaced by human

immunoglobulin molecules (see page 19, lines 31 to page 21, lines 32). The Examiner further stated that claims 80 and 82-87 are drawn to the epitope comprising specific amino acid sequences. The Examiner stated that although Wu et al. I do not specifically teach the amino acid sequences within the epitopes at the N-terminus and the second extracellular loop, it is known in the art that the specific amino acids in claims 81, 82-87 exist in these CCR5 regions as evidenced by Chen et al. (Journal of Virology. 1997; 71(4):2705-2714, see especially page 2708). The Examiner stated that therefore, the monoclonal antibodies 5C7, 3A9, and 2D7 of Wu et al. I bind to CCR5 epitopes that inherently possess the claimed amino acids.

In response to these rejections, Applicants submit that the cancellation, without disclaimer or prejudice, of claims 78-97 renders the rejection of claims 78-88, 90, 91, 93, 94 and 97 under 35 U.S.C. §102 (a) over Wu et al. I moot. Without conceding the validity of the basis of the Examiner's rejection, moreover, Applicants have replaced, inter alia, claims 78-88, 90, 91, 93, 94 and 97 with new claims 100-116 which are believed to distinguish the invention from the Wu et al. I reference. That is, these new claims are not drawn, as indicated in the Office Action (see p.6) to any monoclonal antibody that (1) binds to the N-terminus and/or one of three extracellular loops of CCR5 and (2) is humanized by incorporation of a human immunoglobulin framework. Rather, the new claims (i.e., 100-116) are directed to specific antibodies (or fragments thereof) which bind a single conformational epitope that comprises the N-terminus and the second extracellular loop of CCR5. As stated on page 10 of the Office Action, antibodies having such specificity are not taught or suggested by the prior art, i.e., including Wu, et al. I.

The Examiner points to the teaching in Wu, et al. I of a

bispecific antibody that binds to the N-terminus and the second extracellular loop of CCR5. Wu, et al. I teach that a bispecific antibody has the same or similar epitope specificity as at least two of the antibodies described (p. 15, lines 27-30) i.e., the bi-specific antibody recognizes two different epitopes in which one arm of an Fab would have specificity for one epitope and the other arm of a Fab would have specificity for a different epitope. Applicants respectfully submit that such a bispecific antibody fails to anticipate the antibody of the present invention.

The antibody of the present invention, in contrast to a bispecific antibody in accordance with Wu, et al. I, is monoclonal or monospecific, i.e., it recognizes one epitope on CCR5. The antibody of claims 100-116 recognizes and binds to a single conformational epitope that comprises non-contiguous amino acid sequences, i.e., one amino acid sequence in the N-terminus and an amino acid sequence in the second extracellular loop of CCR5.

For the reasons above, therefore, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 78-88, 90, 91, 93, 94 and 97 under 35 U.S.C.§102(a) over Wu et al. I.

Further to the above, claims 78-83 and 88 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Wu et al., J. Exper. Med., October 1997; 186(8), 1373-1381 (Wu et al. II).

The Examiner stated that the claims are drawn to a monoclonal antibody that binds to the N-terminus or one of the three extracellular loops of CCR5.

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The Examiner further stated that Wu et al. II teaches a monoclonal antibody, murine IgG1 2D7, which binds to the second extracellular loop of CCR5 and another monoclonal antibody, 3A9, which binds to the N-terminal region of CCR5, citing to the second paragraph of the second column on page 1374 and the paragraph bridging the columns on page 1375. The Examiner stated that although Wu et al. II do not specifically teach the amino acid sequence within the epitopes at the N-terminus and the second extracellular loop, it is known in the art that the specific amino acids in claims 80, 82-83 exist in these CCR5 regions, as evidenced by Chen et al. (Journal of Virology. 1997;71(4):2705-2714, citing to page 2708). The Examiner stated that therefore, the monoclonal antibodies 3A9 and 2D7 of Wu et al. II bind to CCR5 epitopes that inherently possess the claimed amino acids.

In response to these rejections, Applicants submit that the cancellation, without disclaimer or prejudice, of claims 78-97 renders moot the rejection of claims 78-83 and 88 under 35 U.S.C. §102(b) over Wu et al. II. Without conceding the validity of the basis of the Examiner's rejection, moreover, Applicants have replaced, inter alia, claims 78-83 and 88 with new claims 100-116 which distinguish the invention from the Wu et al. II reference (as well as from Wu et al. I). These new claims are not, as indicated in the Office Action (see p. 7) drawn to any monoclonal antibody that binds to the N-terminus or one of three extracellular loops of CCR5. Rather, these new claims are directed to specific antibodies (or fragments thereof) which, e.g., bind a single conformational epitope that comprises a first sequence in the N-terminus and the other sequence in the second extracellular loop of CCR5, such as the epitope recognized by antibody PA14 (ATCC accession No. HB-12610). As noted in the

Office Action (see p.10) the antibodies which are the subject of Applicant's presently pending claims are not taught or suggested by the prior art, i.e., including Wu et al. II.

For the reasons above, therefore, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 78-83 and 88 under 35 U.S.C.§102(b) over Wu et al. II.

Rejections Under 35 U.S.C.§103

Claims 84-87 are rejected under 35 U.S.C.§103(a) as allegedly unpatentable over Wu et al. II and further in view of Hill et al., Virology, September 1998; 248:357-371.

The Examiner stated that the claims are drawn to a monoclonal antibody to CCR5 that binds an epitope at the N-terminus and the second extracellular loop of CCR5.

The Examiner further stated that Wu et al. II does not teach a monoclonal antibody with specificity to an epitope on both the N-terminus and the second extracellular loop of CCR5, but does teach monoclonal antibodies that separately bind to each of these regions.

The Examiner also stated that one of ordinary skill in the art at the time the invention was made would have been motivated to make a specific antibody that binds to the N-terminus and the second extracellular loop of CCR5 to effectively inhibit HIV virus entry and inhibit any HIV virus that binds to either or both epitopes. The Examiner stated that one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of producing the claimed invention because Hill et al. teaches that the N-terminus of CCR5 plays an

essential role in the entry of diverse HIV envelope proteins. The Examiner stated that Wu et al. II teaches that the second extracellular loop of CCR5 is an ideal target site for HIV inhibitors and that efficient inhibition of HIV is achieved by monoclonal antibody recognition of either the second extracellular loop or the N-terminus of CCR5. The Examiner stated that therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

In response to the above-discussed rejection of claims 84-87 under 35 U.S.C.§103(a), Applicants submit that the cancellation of claims 78-97, i.e., including that of claims 84-87, renders the §103(a) rejection of those claims moot. New claims 100-116 added to the present application are not drawn to a bispecific antibody to CCR5 that binds an epitope at the N-terminus and binds a different linear epitope in the second extracellular loop of CCR5. Rather, these new claims are directed to monoclonal, monospecific antibodies which, as stated in the Office Action (at p.10) are neither taught nor suggested by the prior art.

As discussed above regarding Wu, et al. I, if one skilled in the art were motivated to construct a bispecific antibody from the antibodies disclosed in Wu, et al. II, the resulting bispecific antibody would not be equivalent to the monoclonal, monospecific antibody of the present invention since the latter antibody binds a single conformational epitope. One skilled in this art would not expect a bispecific antibody to function equivalently to the monoclonal, monospecific antibody of the present invention. Claims 105, 106 and 108-116 recite certain of the desirable characteristics of the monoclonal antibodies of the present invention. One of these characteristics is the ability to inhibit HIV-1 infection of a CD4+ CCR5+ target cell. The prior art

antibodies disclosed in Wu, et al. II do not meet the limitations of these claims. The antibodies 5C7 and 3A9 do not broadly or effectively block HIV-1. Wu, et al. II state that 3A9 is ineffective in blocking HIV-1 entry on U87-CD4-CCR5 cells (see p. 1378, 2nd column, lines 3-4). This is in sharp contrast to the antibodies of the present invention which effectively inhibit fusion of HIV-1 to the same CD4+ CCR5+ cells, as shown in Figures 3, 6A and 6B of the present application.

At the concentration of antibody that inhibits fusion, the antibodies of the present invention do not antagonize the activity of CCR5 in response to a chemokine. This characteristic is recited in claims 105, 106 and 108-115 and may be contrasted to the characteristics of another antibody disclosed in Wu, et al. II, i.e., 2D7, which, at comparable concentrations does antagonize the activity of CCR5 in response to a chemokine (see, e.g., Figure 5B). There is no evidence to suggest that a bispecific antibody comprising 2D7 would not antagonize the activity of CCR5 in response to a chemokine.

For the reasons above, therefore, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 84-87 under 35 U.S.C. §103(a).

Claims 90-97 are rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Wu et al. II.

The Examiner stated that the claims are drawn to a humanized form of the instant monoclonal antibody that binds to the N-terminus or the second extracellular loop of CCR5 and product-by-process construction of the humanized antibody.

The Examiner stated that Wu et al. II does not teach a humanized

form of the monoclonal antibody 2D7 or 3A9. The Examiner stated that one of ordinary skill in the art at the time the invention was made would have been motivated to humanize the monoclonal antibody of Wu et al. II to characterize host immune response and antibody efficiency and effectiveness for use in *in vivo* assays. The Examiner stated that a humanized form of the monoclonal antibody of Wu et al. II would have the added advantage of eliciting a diminished immune response against the recombinant antibody, while retaining the desired functional capacity of reacting with the specific epitope. The Examiner stated that one of ordinary skill in the art would have been motivated to use the human immunoglobulin framework to maintain the conformation of the CDR region from the non-humanized form. The Examiner stated that one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of producing a humanized antibody of Wu et al. II because conventional techniques for humanizing antibodies are known in the art. The Examiner stated that therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

In response to the rejection of claims 90-97 under 35 U.S.C. §103(a) as discussed above, Applicants submit that the cancellation of claims 78-97, including nos. 90-97, renders the §103(a) rejection of those claims moot. New claims 100-116 are not drawn to the humanized form of <u>any</u> antibody falling within the scope of claims 78-89. Rather, the new claims are directed to specific humanized, monoclonal, monospecific antibodies that bind a conformational epitope as discussed above. The antibodies of the present invention, having the defined characteristics as described herein, are neither taught nor suggested by the prior art.

Claims 92, 95 and 96 are rejected under 35 U.S.C. §103(a) over Wu et al. I or, in the alternative, over Wu et al. II.

The Examiner stated that the claims are drawn to monoclonal antibodies containing a framework from a human immunoglobulin IgG1, IgG2, IgG3, IgG4, IgA or IgM.

The Examiner stated that neither Wu et al. I nor Wu et al. II teaches the framework of the monoclonal antibodies to be IgG1, IgG2, IgG3, IgG4, IgA, or IgM. The Examiner stated that, however, it would have been obvious for one of ordinary skill in the art at the time the invention was made to obtain the antibody framework from any of the human immunoglobulins to maintain the conformation of the CDR region and to render the recombinant less immunogenic once administered. The Examiner stated that one of ordinary skill in the art would have been motivated to maintain the donor amino acid sequences immediately adjacent to the CDR domains to assure that when the framework portion of the antibody is added, the CDR domain remains intact. The Examiner also stated that one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of producing the claimed invention because humanizing antibodies using human IgG is a conventional technique for humanizing recombinant antibodies. The Examiner thus concluded that therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

In response, Applicants note that the cancellation of claims 78-97, including inter alia, claims 92, 95 and 96, renders moot the rejection of the subject claims under 35 U.S.C. §103(a). Moreover, as new claims 100-116 are, as noted above, directed to antibodies which are neither taught or suggested by the prior art, the invention recited in these new claims is clearly not

obvious over either Wu et al. I or Wu et al. II, taken alone or in combination.

The Examiner is thus respectfully requested to reconsider and withdraw the rejection of claims 92, 95 and 96 under 35 U.S.C. §103(a).

Summary

For all of the reasons set forth above, therefore, the Examiner is respectfully requested to withdraw all of the objections and rejections set forth in the Office Action and to permit claims 98 and 99 as amended, and new claims 100-116 to proceed to issuance.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

No fee, except the $460.00 fee for a three month extension of time is believed to be due with this amendment. However, if any additional fee is required, authorization is hereby provided to charge the required amount due to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Mark A. Farley 9-13-02

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